ACC.12
61st Annual Scientific Session & Expo
ACC-i2 with TCT innovation in intervention

E775
JACC March 27, 2012
Volume 59, Issue 13

Congenital Cardiology Solutions

INTERIM RESULTS USING TARGETED BIOLOGIC INHIBITION IN CHILDREN WITH MULTIVESSEL INTRALUMINAL PULMONARY VEIN STENOSIS TO ARREST MYOFIBROBLASTIC ACTIVITY

ACC Moderated Poster Contributions
McCormick Place South, Hall A
Sunday, March 25, 2012, 9:30 a.m.-10:30 a.m.

Session Title: Congential Cardiology Solutions: Therapy
Abstract Category: 28. Congenital Cardiology Solutions: Therapy
Presentation Number: 1139-300

Authors: *Sowmya Balasubramanian, Mark W. Kieran, Kimberlee Gauvreau, Christopher Baird, Muneeb Muhammad, Kerry McEnaney, Bethany Trainor, Maliha Rehman, Laureen Sena, Steven Colan, Kathy Jenkins, Children's Hospital Boston, Boston, MA, USA, Harvard Medical School, Boston, MA, USA*

Background: Intraluminal pulmonary vein stenosis (PVS) is a progressive condition in children with high mortality. Neoproliferation of myofibroblasts is the putative mechanism of luminal obstruction. We have previously demonstrated expression of vascular endothelial and platelet derived growth factor receptor in lesions. After encouraging results in pilot studies using Gleevec® and Avastin® to arrest myofibroblast activity, we initiated a prospective investigational new drug study, and report interim findings.

Methods: Patients with multivessel (> 1 vessel) intraluminal PVS in association with congenital heart disease and/or lung disease were anatomically palliated with surgery or transcatheter balloon dilation and treatment with Gleevec® (340mg/m2) was initiated. Patients with primary lung disease also received Avastin® (10mg/kg). Disease activity was monitored monthly using echocardiography and lung scans, with catheter intervention for recurrent obstruction. Patient and vessel status was assessed at baseline and at 6 month intervals, by computed tomorgraphy angiography, and at intervening catheterization, using a predefined scoring system. Drug toxicity was assessed by biweekly blood testing. Adverse events were classified according to the Chemotherapy Clinical Toxicity definitions, and attribution was assigned by a Data and Safety Monitoring Board.

Results: Between 03/2008 and 10/2011, 17 patients were enrolled and treated (2 subsequently withdrew). The median age at diagnosis of PVS was 4 m (0-21) and initiation of drug therapy was at 10 m (1-55). The median time since enrollment is 15 m (4-32). Of the 15 enrolled patients (13 Gleevec, 2 Gleevec and Avastin), 10 are currently receiving treatment, 3 completed treatment (2 at time of transplant), 1 electively ceased treatment due to early stabilization and 1 died. One patient died and 1 survived after transplantation. PVS recurred locally in 11 patients, progressed in 2 and remained stable in 2. No serious adverse events possibly or definitely related to chemotherapy have occurred.

Conclusions: Interim results using targeted biologic agents to suppress myofibroblasts have shown good drug tolerability and early survival.